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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,797	05/16/2001	James L. Hartley	IVGN 192.2 CON	2106
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EXAMINER VOGEL, NANCY TREPTOW				
ART UNIT		PAPER NUMBER		
1636				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/855,797

Applicant(s)

HARTLEY ET AL.

Examiner

NANCY VOGEL

Art Unit

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 March 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 114, 115, 117, 122, 123 and 125-129 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 114, 115, 117, 122, 123, 125-129 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Claims 114, 115, 117, 122, 123, 125-129 are pending in the case.

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection that were not necessitated by applicants' amendment and therefore, this action is final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 114, 115, 117, 122, 123, 125 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the invention as now claimed: "do not recombinant with each other". This a new matter rejection. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned limitations, as currently recited. The specification recites that the molecules "do not substantially recombine with each other". The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such

limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

The following is a new rejection necessitated by applicant's amendment:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 114, 115, 117, 122, 123, 125-129 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyd (Nucleic Acids Research 21(4):817-821, 1993; of record) in view of Fox et al. (US Patent 6,140,086; of record) and Sadowski et al. (J. Bacteriol. 165, 341-347, 1989) or Sadowske et al. (FASEB J. 7, 760-767, 1993).

Boyd teaches an in vitro method for high-speed cloning comprising producing one or more product nucleic acid molecules comprising two or more lox sites, the method comprising:

(a) generating a linear nucleic acid molecule; and

(b) contacting the linear nucleic acid molecule with (i) on or more "adapters" comprising one or more lox sites and (ii) a DNA ligase, under conditions sufficient to add one "adapter" to each terminus of the linear nucleic acid molecule, thereby producing the product nucleic acid molecule (see entire document, especially page 818 and Figure 2). With regard to claim 117, 125, 128, Boyd teaches that blunt-ended fragments could be produced by PCR amplification or by cDNA synthesis (see page 817, column 1 and page 82, second paragraph). Regarding claim 129, on page 817 Boyd teaches the use of nucleic acids with Sall ends. Regarding claims 126-129, Boyd teaches that the lox sites added to either end of the linear nucleic acid can be the same (i.e., the same sequence in the same orientation) or different (i.e. the same sequence in reverse orientation) (see e.g., page 819, Figure 2).

Boyd does not teach this procedure wherein topoisomerase is used as the DNA ligase to add the adapters to each terminus of the linear nucleic acid molecule thereby producing the product nucleic acid molecule, and does not teach the procedure using adapters or linear DNA comprising att sites such as attB, attP, attL or attR.

However, Fox et al. teach methods and compositions for high-efficiency, rapid cloning of nucleic acids, including methods for inserting amplified nucleic acids of interest into a vector (see entire document, especially columns 5-8). Fox et al. teach that, like T4 DNA ligase, topoisomerase can be used to ligate amplified, synthesized or digested nucleic acid molecules (see entire document, especially column 11, lines 56-61; column 7, lines 41-45; and column 18, lines 17-25). Sadowske (J. Bacter.) or Sadowski (FASEB J) each disclose the common features of site-specific recombinases

such as lambda Int and P1 Cre, as well as their action on specific sites att and lox (see pages 763-764, in Sadowski (FASEB J), see page 341 of Sadowski (J. Bacter.).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute in vitro recombination performed by topoisomerase as taught by Fox et al. in the method of synthesizing one or more nucleic acid molecules as taught by Boyd because Fox et al. teach that it is within the skill of the art to utilize T4 DNA ligases as well as topoisomerases to recombine DNA, especially to ligate an insert into a vector, and Boyd teaches that it is within the skill of the art to synthesize one or more linear nucleic acid molecules to add one more "adapters" comprising one or more lox sites to each end of the linear nucleic acid in order to achieve rapid and efficient cloning of a nucleic acid of interest. It would have been further obvious to utilize att sites in the adapters in the place of lox sites since Sadowski (J. Bacter.) and Sadowski (FASEB J.) teach that the Int/att and Cre/lox systems are members of a common family of enzyme systems having similar properties of site specific recombination activity. It would have been further obvious to one of ordinary skill in the art to have used any combination of att and lox sites, for manipulation of DNA fragments, including the use of sites on a first molecule which do not recombine with each other, in order to obtain the desired final DNA product, since it was taught in the references that att sites and lox sites can be used for constructing nucleic acid molecules of choice, and since the recombinant properties of each att and lox sites were well known in the art and taught by the references. One of ordinary skill in the art would have been motivated to substitute the use of topoisomerase as taught by Fox et al., and the att and/or lox sites

in the adapters as taught by either of Sadowski (J. Bact) or Sadowski (FASEBJ), in the method as taught by Boyd simply as a matter of designer's choice since both T4 DNA ligase and topoisomerase would serve the same purpose, and att sites and lox sites would serve the same purpose, in Boyd's method of turbo cloning. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success when using a topoisomerase instead of a T4 DNA ligase as taught by Fox et al., and att sites instead of lox sites as taught by each of Sadowski, in Boyd's method of attaching nucleic acids comprising one or more lox sites to each end of a first linear nucleic acid.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
5/11/09

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